

CLAIMS AS CURRENTLY PENDING

SERIAL NO. 09/334,969

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E 1  
1. A synthetic multivalent T cell receptor (TCR) complex for binding to a MHC-peptide complex, which TCR complex comprises a plurality of T cell receptors specific for the MHC-peptide complex, wherein each TCR in the complex is a refolded recombinant TCR which comprises:

- D 1
- i.) a recombinant TCR  $\alpha$  or  $\gamma$  chain extracellular domain having a first C-terminal dimerization peptide which is heterologous to the  $\alpha$  or  $\gamma$  chain; and
  - ii.) a recombinant TCR  $\beta$  or  $\delta$  chain extracellular domain having a second C-terminal dimerization peptide which is specifically heterodimerized with the first heterodimerization peptide to form a heterodimerization domain,

wherein a disulfide bond present in native TCRs between the  $\alpha$  and  $\beta$  or  $\gamma$  and  $\delta$  chains adjacent to the cytoplasmic domain is absent from the recombinant TCR.

2. The TCR complex according to claim 1, wherein the T cell receptors are  $\alpha\beta$  T cell receptors having an  $\alpha$  chain and a  $\beta$  chain.

3. The TCR complex according to claim 2, wherein the  $\alpha$  chain and  $\beta$  chain are soluble forms of T cell receptor  $\alpha$  and  $\beta$  chains.

4. The TCR complex according to claim 1, wherein the T cell receptors are in the form of multimers of two or more T cell receptors.

5. The TCR complex according to claim 4, wherein the multimer is a trimer or a tetramer.

6. The TCR complex according to claim 1, wherein the T cell receptors are associated with one another via a linker molecule.

E 2  
D 2  
7. The TCR complex according to claim 6, wherein the linker molecule is a multivalent attachment molecule.

8. The TCR complex according to claim 7, wherein at least one of the T cell receptor  $\alpha$  or  $\beta$  chains is derived from a fusion protein comprising an amino acid sequence encoding a protein tag.

9. The TCR complex according to claim 8, wherein the T cell receptors are biotinylated.

E3  
D3 10. The TCR complex according to claim 1, comprising a multimerized recombinant T cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T cell receptor heterodimer.

E<sup>m</sup>  
D4 11. A multivalent TCR complex comprising a multimerized recombinant T cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T cell receptor heterodimer, wherein each TCR in the complex is a refolded recombinant TCR which comprises:

- i) a recombinant TCR  $\alpha$  or  $\gamma$  chain extracellular domain having a first C-terminal dimerization peptide which is heterologous to the  $\alpha$  or  $\gamma$  chain; and
- ii) a recombinant TCR  $\beta$  or  $\delta$  chain extracellular domain having a second C-terminal dimerization peptide which is specifically heterodimerized with the first dimerization peptide to form a heterodimerization domain,

wherein a disulfide bond present in native TCRs between the  $\alpha$  and  $\beta$  or  $\gamma$  and  $\delta$  chains adjacent to the cytoplasmic domain, is absent from the recombinant TCR.

E4  
DS- 14. The TCR complex according to claim 11, wherein the heterodimerization domain is a coiled coil domain.

15. The TCR complex according to claim 14, wherein the dimerization peptides are c-jun and c-fos dimerization peptides.

16. The TCR complex according to claim 11, comprising a flexible linker located between the T cell receptor chains and the heterodimerization peptides.

17. The TCR complex according to claim 1, wherein the T cell receptor is expressed in an *E. coli* expression system.

18. The TCR complex according to claim 1, wherein the T cell receptor is biotinylated at the C-terminus.

19. The TCR complex according to claim 1, wherein the T cell receptors are associated with a lipid bilayer.

20. The TCR complex according to claim 19, wherein the lipid bilayer forms a vesicle.

21. The TCR complex according to claim 20, wherein the T cell receptors are attached at the exterior of the vesicle.

E5  
D6 22. The TCR complex according to claim 20 or claim 21, wherein the T cell receptors are attached to the vesicle via derivatized lipid components of the vesicle.

23. The TCR complex according to claim 19 or claim 20, wherein the T cell receptors are embedded in the lipid bilayer.

D7 E5 24. The TCR complex according to claim 1, wherein the T cell receptors are attached to a solid structure.

25. The TCR complex according to claim 1, further comprising a detectable label.

26. The TCR complex according to claim 1, further comprising a therapeutic agent such as a cytotoxic agent or an immunostimulating agent.

27. The TCR complex according to claim 1, in a pharmaceutically acceptable formulation for use *in vivo*.

33. The TCR complex according to claim 1, wherein the heterodimerization domain is a coiled coil domain.

34. The TCR complex according to claim 33, wherein the dimerization peptides are c-jun and c-fos dimerization peptides.

35. The TCR complex according to claim 1, comprising a flexible linker located between the T cell receptor chains and the heterodimerization peptides.

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